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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,722	11/14/2003	Xian-Ping Lu	4865-104 US	2070

7590 04/24/2006

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EXAMINER	
SEAMAN, D MARGARET M	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/713,722	LU ET AL.	
	Examiner	Art Unit	
	D. Margaret Seaman	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application was filed 11/14/2003 and claims benefit of Provisional Application 60/429,294 (11/26/2002). Claims 1-19 are before the Examiner.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. The rejection of claims 13-19 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained for reasons of record. Applicant argues that the PPAR are well known in the art to mediate type 2 diabetes and many other conditions. Also, it is a well-established and routine art-accepted protocol to evaluate a candidate agent's agonistic activity of PPAR by means of a cell-based assay. Many different biological pathways have been connected in some way to treating every condition of the body from hair loss to ingrown nails. However there is a difference of having a link between a biological activity and providing a written description of how PPAR mediation can/has treated conditions such as syndrome X, which is very hard to diagnose and mimics the same conditions as allergies, arthritis, and AIDS.

3. The rejection of claims 13-19 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is maintained for reasons of record. (see office action dated 6/24/2005). Applicant argues that PPAR are well known in the art to mediate many conditions. Those of skill in the art recognize that in vitro assays and or cell-cultured based assays are generally useful to observe basic physiological and cellular phenomenon such as screening the effects of potential drugs. However, clinical correlations are generally lacking. The greatly increased complexity of the in vivo environment as compared to the very narrowly defined and controlled conditions of an in- vitro assay does not permit a single extrapolation of in vitro assays to human diagnostic efficacy with any reasonable degree of predictability. In vitro assays cannot easily assess cell-cell interactions that may be important in a particular pathological state. Furthermore it is well known in the art that cultured cells, over a period time, lose phenotypic characteristics associated with their normal counterpart cell type. Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). The reference states that evidence of the contradictions between life on the bottom of a lab dish and

in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in cell-cell interactions. Applicant has shown that the instantly claimed compounds have in vivo lowered the blood glucose levels and lowered blood triglyceride levels. Claims directed to such treatment (type 2 diabetes and dyslipidemia) would be considered in a more favorable light.

4. The rejection of claims 1-19 under 35 U.S.C. 112, first paragraph, as failing to comply with the scope of enablement requirement, is maintained for reasons of record. Applicant argues that many different compounds have written description in the specification. However, the only compounds made by the instant specification have A ring being cyclohexyl, benzene or pyridine; B being Benzene; Ar being benzene, X and Y being O; and R1, R2, R3, R4 and R5 being H or alkyl only. Only two compounds have been tested for activity as either lowering blood glucose levels or lowering blood triglyceride levels. This does not enable the full scope of the compounds provided by the instant claim 1.

This rejection can be overcome by amended the claims such that the different variables are more in line with the compounds made and tested.

NEW REJECTIONS

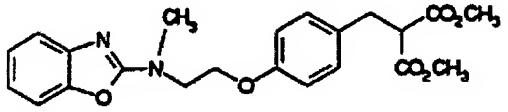
Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

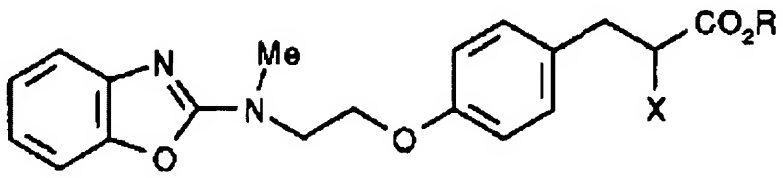
6. Claims 1-19 are rejected under 35 U.S.C. 102(b) as being anticipated by WO

Dimethyl 2-[4-[2-[N-(2-benzoxazolyl)-N-methylamino]ethoxy]-phenylmethyl]propane-1,3-dioate



9413650. Wo teaches as a pharmaceutical to treat several disorders that fall within the scope of the instant claims.

7. Claims 1-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Buckle.



1 (X = Hal, SR^1, NR^1R^2, OR^1);
SB 213068 (X = OEt, R = H);
2-20

Buckle teaches compound 2

Compound	X	R	ED_{25} ($\mu mol.kg^{-1}$ diet)[b]
2	CO_2Me	Me	10

As an antidiabetic agent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. Margaret Seaman whose telephone number is 571-272-0694. The examiner can normally be reached on 730am-4pm, Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecelia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

D. Margaret Seaman
Primary Examiner
Art Unit 1625

dms